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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
MYERS, CARLA J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/250,883	RUSSELL ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114.

Applicant's submission filed on April 14, 2003 has been entered.

This action contains new grounds of rejection and is made non-final.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25-34 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific or well-established utility.

The claims are drawn to polynucleotides consisting of a sequence selected from the group consisting of SEQ ID NO: 1-14 and recombinant expression systems comprising an isolated and purified nucleic acid sequence having an open reading frame operably linked to a control sequence wherein the nucleic acid sequence is selected from the group consisting of SEQ ID NO: 1-14 and equivalent degenerate coding sequences. The claimed polynucleotides are not supported by either a specific and substantial asserted utility or a well-established utility. The

specification fails to provide objective evidence of any activity for the claimed polynucleotides or to show that polynucleotides having the stated consensus sequence of SEQ ID NO: 14 even exist. The specification teaches that a consensus sequence derived from SEQ ID NO: 1-13 hybridizes to ESTs in 27% of breast tissue samples, whereas the consensus sequence only hybridizes to ESTs in 3.4% of non-breast tissue samples. Based on this information, the specification concludes that the individual sequence fragments of SEQ ID NO: 1-13 and the consensus sequence of SEQ ID NO: 14 are useful in "detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating or determining the predisposition to, disease and conditions of the breast, such as breast cancer" (see page 10 of the specification). However, the specification provides no evidence that the sequences of SEQ ID NO: 1-14 are correlated with any type of disease or condition of the breast. There is no information provided in the specification regarding the level of expression of SEQ ID NO: 1-14 in any type of diseased breast tissue. The finding that mRNAs which hybridize to SEQ ID NO: 14 are more prevalent in breast tissue than in normal tissue does not indicate that such sequences are associated with diseases or conditions of the breast. Furthermore, the finding that mRNAs which hybridize to SEQ ID NO: 14 are more prevalent in breast tissue rather than normal tissues does not indicate that mRNAs which hybridize to any one of SEQ ID NO: 1-13 are also more prevalent in breast tissue because there is no evidence concerning the hybridization properties of the individual nucleotide fragments. The specification suggests that the claimed polynucleotide could be used for therapeutic purposes. Clearly, further research would be required to identify a disease for which the protein encoded by SEQ ID NO: 1-14 is involved and for which treatment with SEQ ID NO: 1-14 or any nucleic acid having 90% identity with SEQ ID NO: 1-14 would be effective

or for which detection of SEQ ID NO: 1-14 expression would be informative. As stated in Brenner v. Manson, 383 U.S. 519 535-536, 148 USPQ 689, 696 (1966) " a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Support for an asserted utility that is specific and substantial would require, for example, a showing of a particular function for an encoded polypeptide. Merely identifying and studying the properties of a polypeptide or the diseases in which a polypeptide or polynucleotide may be involved does not constitute a "real world" context of use. Moreover, the use of the claimed polynucleotide to detect breast tissue is considered to be a general use, rather than a specific use since tissue specific expression is a characteristic of a large genus of nucleic acids. Accordingly, the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. Applicants attention is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

3. Claims 25-34 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, or credible asserted utility or well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

4. **RESPONSE TO ARGUMENTS:**

In the response of April 14, 2003, Applicants traverse the 101 and 112, first paragraph (enablement) rejections by stating that the claimed sequences can be used as diagnostic markers of breast tissue. Applicants point out that the consensus sequence and fragments thereof are found more than 22 times more often in breast than in non-breast tissue. It is asserted that other tissue markers, such as CEA and PSA are not present in only a single tissue and yet they are still

useful as markers of disease. Applicants further state that the Declaration of Dr. Paula Friedman, submitted with the response of January 11, 2001 has established that BS203 can be used as a tissue specific marker and is capable of acting as a cancer diagnostic.

Applicant's arguments have been fully considered but are not persuasive to overcome the present grounds of rejection. In this response, Applicants have argued that because BS203 is expressed more frequently in breast tissue than in non-breast tissue, BS203 can be used as a marker to detect breast tissue. However, the detection of breast tissue or the identification of a cell as being of breast origin is not considered to be a specific utility. As set forth in the Utility Examination Guidelines, a specific utility is a "utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target." The ability of a nucleic acid to identify a cell type, such as a breast cell, is considered to be characteristic of a broad class of molecules. Therefore, such a utility is not considered to be specific. Further, the specification has not clearly established that SEQ ID NO: 1-14 are in fact specific for breast cells. Applicants have shown that SEQ ID NO: 14 is expressed more frequently in breast tissue than in other tissues, but Applicants have not provided any information regarding the hybridization and expression properties of SEQ ID NO: 1-13, which are subfragments of the consensus sequence of SEQ ID NO: 14. Applicants have previously asserted that SEQ ID NO: 1-14 share identity with GERP and have relied on this information to assert a utility and function for SEQ ID NO: 1-14. As discussed in the previous Office action, Vincent (Exhibit B, cited in the response of Paper No. 22) teaches that GERP is

expressed in normal breast cells, as well as in normal brain, lung, placenta, kidney, muscle and germinal center B cells. Since the present sequences of SEQ ID NO: 1-14 have been asserted to have the same functional properties as GERP, it would follow that these sequences are also expressed in additional tissues and are not in fact specifically expressed in breast cells. Applicants comment regarding the fact that PSA and CEA are not expressed in a single cell type and yet are useful in disease diagnosis is noted. However, the properties of PSA and CEA are clearly distinct from the properties of BS203 nucleic acids and proteins. As acknowledged by Applicants, PSA is expressed at low levels in normal prostates and at high levels in patients with prostate disease. Additionally, CEA is expressed at higher levels in patients with colon disease than in patients without colon disease. However, a similar showing has not been made for BS203. There is no evidence of record to indicate that BS203 is expressed at higher levels in breast cells from patients having diseases of the breast than in breast cells from normal/control patients. Thereby, the finding that GERP-like nucleic acids (which nucleic acids Applicants have asserted include BS203 nucleic acids) are expressed at similar levels in normal breast tissue as well as in other tissues indicates that these nucleic acids cannot be used as a specific marker of breast tissue and breast disease.

5. Claims 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides comprising a nucleic acid sequence having an open reading frame operably linked to a control sequence wherein said nucleic acid sequence is

selected from the group consisting of SEQ ID NO: 1-13. SEQ ID NO: 14 is a consensus sequence obtained by aligning the overlapping clones of SEQ ID NO: 1-13. However, SEQ ID NO: 1-13 are fragments of this larger sequence and are not themselves open reading frames. While the claims recite the language "consisting of," the claims also recite that the expression system comprises an open reading frame. Accordingly, the broadest reasonable interpretation of the claims indicates that the claims are inclusive of BS203 genes and BS203 genomic sequences which contain SEQ ID NO: 1-13 and additional flanking sequences of undefined identity. However, the specification does not teach any full length BS203 genes or any BS203 genomic sequences. The specification does not teach that any of the nucleic acids span more than one exon, and thereby the claims as written include flanking intron sequences and full length gene sequences. Furthermore, the claims include nucleic acids which are defined only in terms of a small fragment. The claims do not define the sequence of the flanking nucleic acids, nor do the claims include functional language for the nucleic acids. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met

for a genus claim, it is first determined whether a representative number of specifies have been described by their complete structure. In the instant case, the specification does not teach any intron or 5' regulatory or 3' untranslated sequences. The specification also does not teach any additional nucleic acids which comprise the fragments of SEQ ID NO: 1-13. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, chromosomal map position, biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for any of the polynucleotides. While at the time of filing applicants were in possession of polynucleotides consisting of SEQ ID NO: 1-14, the specification provides no information regarding genomic sequences surrounding the sequences of SEQ ID NO: 1-13. Furthermore, the specification does not identify any additional BS203 nucleic acids other than the consensus sequence of SEQ ID NO: 14. The limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of BS203 genomic sequences or nucleic acids comprising SEQ ID NO: 1-13. Therefore, the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. **RESPONSE TO ARGUMENTS:**

In the response of April 14, 2003, Applicants state that the rejection has been overcome by the amendment to the claims to recite "consisting of" in place of "comprising." However, as discussed above, the claims require that the expression system comprises a nucleic acid having

an open reading frame. The nucleic acids of SEQ ID NO: 1-13 are fragments of the larger molecule of SEQ ID NO: 14 and are not themselves complete open reading frames. Accordingly, the claims encompass sequences flanking SEQ ID NO: 1-13 in order to meet the limitation that the expression system has an open reading frame. While the specification describes nucleic acids **consisting of** SEQ ID NO: 1-14, the specification does not adequately describe expression systems comprising a nucleic acid having an open reading frame and consisting of the sequence of SEQ ID NO: 1-14.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION:

7. ***Claim Rejections - 35 USC § 112 Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32 and 33 are indefinite and confusing because the claims are drawn to expression systems comprising an isolated nucleic acid having an open reading frame wherein the nucleic acids are selected from the group consisting of SEQ ID NO: 1-14. Since SEQ ID NO: 1-13 are not full length open reading frames, it is unclear as to whether the claims are intended to be limited to expression systems comprising an open reading frame and containing a nucleic acid consisting of SEQ ID NO: 1-14 or if the claims are intended to be limited to expression systems comprising a nucleic acid consisting of SEQ ID NO: 1-14 and wherein said nucleic acids consist of a fragment of an open reading.

Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 34 is drawn to a method for producing a polypeptide, but recites only a step of incubating a host cell that has been transfected with an expression vector. The claim does not clearly set forth how this incubation the results in the production of a polypeptide. Accordingly, the claim omits an essential step in which the polypeptide is produced.

8.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (f) he did not himself invent the subject matter sought to be patented.

9. Claims 25-30 are rejected under 35 U.S.C. 102(a) as being anticipated by the Incyte LifeSeq™ Database.

The specification at page 52 states that the nucleic acid clones for SEQ ID NO: 1-13 (i.e., clones 2269559, 1664718, 2360586, 1436565, 479125, 2247228, 2112334, 960106, 962045, 959580, 961381, 2517547 and 2124915) were procured from, and thereby known and used by, Incyte Genomics at the time the invention was made. The specific nucleotide sequence is an inherent property of each of these clones. Accordingly, nucleic acids consisting of SEQ ID NO:

1-13, as well as those which could be produced by recombinant techniques or synthetic techniques, were known and used in the art prior to the filing of the present application.

10. Claims 25-30 are rejected under 35 U.S.C. 102(b) as being in public use or on sale.

The specification at page 52 states that the nucleic acid clones for SEQ ID NO: 1-13 (i.e., clones 2269559, 1664718, 2360586, 1436565, 479125, 2247228, 2112334, 960106, 962045, 959580, 961381, 2517547 and 2124915) were procured from, and thereby known and used by, Incyte Genomics at the time the invention was made. The specific nucleotide sequence is an inherent property of each of these clones. Accordingly, nucleic acids consisting of SEQ ID NO: 1-13, were in public use and on sale in this country prior to the filing of the present application.

11. Claims 25-30 are rejected under 35 U.S.C. 102(f) because the applicant did not himself invent the claimed subject matter.

The specification at page 52 states that the nucleic acid clones for SEQ ID NO: 1-13 (i.e., clones 2269559, 1664718, 2360586, 1436565, 479125, 2247228, 2112334, 960106, 962045, 959580, 961381, 2517547 and 2124915) were procured from, and thereby known and used by, Incyte Genomics at the time the invention was made. The specific nucleotide sequence is an inherent property of each of these clones. Accordingly, it appears that Applicant did not invent the claimed subject matter.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over the Incyte LifeSeq™ Database in view of Linskens et al (U.S. Patent No. 5,744,300).

As discussed in the specification at page 52, the clones 2269559, 1664718, 2360586, 1436565, 479125, 2247228, 2112334, 960106, 962045, 959580, 961381, 2517547 and 2124915 were procured from, and thereby known and used by and available from, Incyte Genomics at the time the invention was made. It is a property of these clones that they consist of the nucleotide sequence of SEQ ID NO: 1-13. The cited art does not teach attachment of the polynucleotide to a solid phase.

Linskens teaches that probes comprising EST sequences may be immobilized onto a solid support in order to facilitate hybridization methods and to allow for the detection of cells expressing nucleic acids complementary to said probes. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have immobilized the EST polynucleotides of the Incyte LifeSeq™ Database onto a solid support as taught by Linskens in order to have provided a simple and effective means for detecting expression of the isolated polynucleotides in cell samples.

13. Claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Incyte LifeSeq™ Database in view of Inoue (Proceedings of the National Academy of Sciences (December 1993) 90: 11117-11121).

As discussed in the specification at page 52, the clones 2269559, 1664718, 2360586, 1436565, 479125, 2247228, 2112334, 960106, 962045, 959580, 961381, 2517547 and 2124915 were procured from, and thereby known and used by and available from, Incyte Genomics at the time the invention was made. It is a property of these clones that they consist of the nucleotide sequence of SEQ ID NO: 1-13, respectively. The cited art does not specify that the clones were obtained in an expression system.

However, Inoue teaches cloning polynucleotides into expression vectors, transforming host cells with the resulting recombinant vectors and expressing polypeptides encoded by the polynucleotides using the transformed host cells (see pages 11119-111120). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the polynucleotides of the Incyte LifeSeq™ Database into expression vectors, to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application

may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers
July 15, 2003

CARLA J. MYERS
PRIMARY EXAMINER